

THE ISOLATION AND SYNTHESIS
OF DIHYDROSPHINGOSINE

BY
WILLIAM PENROD NORRIS

B. A., De Pauw University, 1941

AN ABSTRACT OF A THESIS

SUBMITTED IN PARTIAL FULFILLMENT OF THE REQUIREMENTS
FOR THE DEGREE OF DOCTOR OF PHILOSOPHY IN CHEMISTRY
IN THE GRADUATE SCHOOL OF THE UNIVERSITY
OF ILLINOIS, 1944

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ACKNOWLEDGMENT

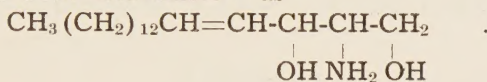
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PART I

ISOLATION OF DIHYDROSPHINGOSINE

INTRODUCTION

Of the lipids occurring in nervous tissue the cerebrosides and sphingomyelins (sphingolipids) are unique in that they are derivatives of a complex base, sphingosine. The structure of sphingosine has been established^{1,2} as



Results have been obtained which make advisable a further investigation of the basic sphingosine fraction from sphingolipid hydrolysates.

EXPERIMENTAL

Bovine brain or spinal cord was ground and extracted successively with acetone, cold ether, and hot alcohol. Sphingolipids precipitated from the alcohol extract on cooling; the product from spinal cord far surpassing that from brain both in purity and quantity. Cerebrosides were obtained by recrystallization from glacial acetic acid. Hydrolysis of the cerebrosides by the method of Klenk and Diebold³ gave sphingosine in amorphous form.

in the recrystallization of crude sphingosine sulfate prepared from brain or spinal cord a fraction was consistently obtained which was nearly insoluble in boiling methyl alcohol. Acetylation of this material with acetic anhydride in 0.5 N sodium hydroxide, using ether containing a small volume of methyl alcohol as a solvent, gave the N-acetyl derivative which was further acetylated in pyridine by the method of Klenk and Diebold³. The product was a white crystalline solid which was identical with triacetyldihydrosphingosine prepared by reducing sphingosine to dihydrosphingosine and acetylating the latter in pyridine.

SUMMARY

Dihydrosphingosine has been shown to exist in considerable quantity in normal bovine nervous tissue. It was isolated from sphingolipid hydrolysates as the more insoluble sulfate and identified through its triacetyl derivative.

BIBLIOGRAPHY

- ¹ Glick, F. J., Ph.D. Thesis, Univ. of Ill., 1943.
- ² Carter, H. E., Glick, F. J., Norris, W. P., and Phillips, G. E., J. Biol. Chem., **142**, 449 (1942).
- ³ Klenk, E., and Diebold, W., Z. physiol. Chem., **198**, 25 (1931).

PART II

SYNTHESIS OF DIHYDROSPHINGOSINE

INTRODUCTION

A method for the synthesis of alkamines by the reduction of esters of α -amino acids with Raney nickel has been reported by Levene et. al.¹ This reaction was investigated as a possible means of synthesizing 1,3-dihydroxy-2-amino compounds and especially the long chain homolog, dihydrosphingosine.

EXPERIMENTAL

The O-ethyl ether of oximino-acetoacetic ester, oximino-acetoacetic ester, *dl*-threonine methyl ester, and *dl*-allothreonine methyl ester were all converted to the corresponding 1,3-dihydroxy-2-amino-butan-2-ols by reduction with large quantities of Raney nickel at 90-95°C. under 2000 pounds pressure of hydrogen. The aminoglycols were isolated in about 60 per cent yields by precipitation from absolute alcohol with oxalic acid. They were also benzoylated in pyridine to give tribenzoyl derivatives.

An attempt was made to prepare methyl α -amino- β -hydroxy stearate by the mercuriation method used by Carter² in the syntheses of threonine and serine. Palmitaldehyde, prepared from palmitoyl chloride by the Rosenmund method³, was condensed with malonic acid⁴ in pyridine to give 2-3-octadecenoic acid. The

unsaturated acid was reacted with mercuric acetate in methyl alcohol to give α -acetomercuri- β -methoxy-stearic acid in almost quantitative yields. Bromination of this material in aqueous potassium bromide, however, was unsatisfactory due to the insolubility of the mercuri- addition complex.

SUMMARY

A method has been devised for the synthesis of 1,3-dihydroxy-2-amino compounds by the catalytic reduction of α -amino- β -hydroxy esters with Raney nickel. Preparations of 2-3-octadecenoic acid and α -acetomercuri- β -methoxy-stearic acid have been described.

BIBLIOGRAPHY

- ¹ Ovakimian, G., Kuna, M., and Levene, P. A., J. Am. Chem. Soc., **62**, 676 (1940).
- ² Carter, H. E., Org. Syn. **20**, 81, 101 (1940).
- ³ Hershberg, E. B., and Cason, J. C., Org. Syn., **21**, 84 (1941).
- ⁴ Goldberg, A. G., and Linstead, R. P., J. Chem. Soc., 2343 (1928).

VITA

The author was born September 2, 1920, in Loogootee, Indiana. He was graduated from Loogootee High School in May, 1937, and entered DePauw University the following September. At the beginning of his second year at DePauw he was awarded a Rector Scholarship and received the degree of Bachelor of Arts in June, 1941. He entered the graduate school of the University of Illinois in September, 1941, as the recipient of a special Research Fellowship granted the University by the Upjohn Pharmaceutical Company. He held this appointment during his first two years of graduate study. During his third year he served as a half-time Assistant in Chemistry.



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